REMARKS

Favorable reconsideration is respectfully requested in view of the following remarks. Applicants sincerely thank the Examiner for holding a telephonic interview with Applicants' representative on November 20, 2009. The Examiner's kind suggestions have been incorporated herein.

Furthermore, Applicants note the cover sheet to the Office Action dated August 7, 2009 indicates that this Office Action is both a final Office Action and a non-final Office Action. The Applicants' representative has confirmed by telephone with the Examiner that this Office Action is actually a non-final Office Action.

I. CLAIM STATUS AND AMENDMENTS

Claims 1-27, 29 and 33-46 were pending in this application when last examined.

Claims 1, 2 and 35 were examined on the merits and stand rejected.

Claims 3-27, 29, 33, 34 and 36-46 were withdrawn as non-elected subject matter.

II. ENABLEMENT REJECTIONS

On pages 2-3 of the Office Action, claims 1, 2 and 35 were rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification lacks enablement. Applicants respectfully traverse this rejection for the reasons of record and for the following reasons.

Initially, regarding the Enablement rejection, the previous Office Action refers to Nakamura, 2000. However, in the previous response, we asserted arguments based on Nakamura, 2002. In particular, Nakamura 2002 teaches DANCE (fibulin -5) binding to αvβ3, αvβ 5 and a α9β1. For instance, see the top bold paragraph on pg 172 of Nakamura 2002. In fact, such reference teaches that DANCE serves as a ligand for these integrins through its amino-acid terminal domain. Claimed SEQ ID NO: 6 corresponds to the 24- 77 AA in DANCE and thus corresponds to this amino region.

Further, Reference Example 1 of the specification (starting on page 63) is in part directed towards DANCE with the portion corresponding to SEQ ID NO 6 deleted. Such deletion resulted in loss of binding to αvβ3, αvβ5 and α9β1.

Finally, looking at Reference Example 1, it is noted that the RGD motif appears to be important for binding to αvβ3, αvβ5 and α9β1 as a single mutation in this motif results in a large

reduction in binding and deletion of this motif results in no binding. Thus, Applicants have provided a structure to guide a person of art to practice the claimed invention without undue experimentation.

Thus, the present application and Nakamura 2002 together demonstrate that SEQ ID NO: 6 can bind αvβ3, αvβ5 and α9β1. The reference Van der Fliers, cited in the rejection, does not seem applicable.

Furthermore, Applicants note that the genus of human αvβ3, αvβ5 and α9β1 integrins is very small and highly homologous as shown by the attached references.

Fornaro et al. (Matrix Biology, Vo1.16, pp.185-193, 1997) (Attachment A) and de Melker et al. (BioEssays, vol.21, pp.499-509, 1999) (Attachment B) disclose that βI and 3 integrins share only 4 (or 5) and 2 (or 3) cytoplasmic splice variants, respectively (Fornaro et al., page 186, Table 1 /de Melker et al., page 501, Table 2, and page 502, right column, lines 4 to 38). Further, Fornaro et al. discloses that differences in the cytoplasmic domain do not affect either aβ heterodimer formation or the ligand specificity (page 185, Abstract).

de Melker et al. further discloses that there is one 60 kDa truncated form of β3 integrin which consists of the 404 N-terminal extracellular residues of β3 followed by 23 residues encoded by intronic sequences (page 501, right column, lines 4 to 8).

de Melker et al. also discloses that no splice variants for human β5 integrin have been detected (page 503, left column, lines 7-9). This is also supported by the information relating to human β5 integrin gene entered in the latest NCBI database. According to the information of ITGB5 integrin, beta 5 in the NCBI Gene database, only one kind of human β5 integrin gene transcript, NM_002213.3, is registered (see Entrez gene, select 3693) (Attachment C). The date of first entry of NM_002213 into NCBI is March 24, 1999 (see Revision history for NM_002213.3) (Attachment D).

Similarly, as a transcript for human α9 integrin gene, only one kind of transcript NM_002207.2 encoding a protein specified by NP_002198.2 is registered (see Entrez gene, select 3680) (Attachment C). The date of first entry of NM_002207 into NCBI is November 23, 2000 (see Revision history for NM_002207.2) (Attachment E).

In contrast, as transcripts for human αv integrin gene, three kinds of transcripts including NM_002210.3, NM_001145000.1 and NM_001144999.1 are registered (see Entrez gene, select 3685) (Attachment C). However, the date of first entry of each sequence is March 24, 1999,

February 12, 2009, and February 12, 2009, respectively, and therefore, the transcript variant for human αv integrin known before the priority date of the present application is only NM_002210.3 (Attachment F-H).

From the foregoing, it is clear that, before the priority date of the present application, 4 (or 5) and 2 (or 3) kinds of cytoplasmic splice variants were known for human β1 and β3 integrins, respectively; in addition, it was considered that differences in the cytoplasmic domain do not affect the ligand specificity, only one kind of a truncated form having different extracellular domain was known for human β3 integrin, and only one kind of transcript was known for human β5, α9 and αv integrins.

Therefore, at the time of filing, the genus of human αvβ3, αvβ 5 and αvβ1 integrins was very small and highly homologous.

Thus, it is clear to a person of skill in the art that the specification teaches that the RGD motif appears to be important for binding. Furthermore, the art teaches that at the time of filing, only a very limited number of the claimed integrins were known. Thus, applicants respectfully suggest, that at the time of filing a person of skill in the art would have practiced the claimed invention based on the specification and the knowledge in the art without undue experimentation. Thus, Applicants respectfully suggest that this rejection is untenable and should be withdrawn.

III. WRITTEN DESCRIPTION REJECTION

On pages 3-4 of the Office Action, claims 1, 2 and 35 were rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification fails to comply with the written description requirements. Applicants respectfully traverse this rejection.

As noted above, the specification sets forth that the RGD motif appears to be important for binding to the claimed integrins as a single mutation in this motif results in a large reduction in binding and deletion of this motif results in no binding. Further, the present application and Nakamura 2002 together demonstrate that SEQ ID NO: 6 can bind αvβ3, αvβ 5 and αvβ1. Also, the attached references show that the genus of these integrins known at the time of filing was very small. Thus, Applicants respectfully suggest that the teachings in the specification and the knowledge in the art indicate that Applicants had possession of the claimed invention at the time of filing.

Furthermore, with regard to the limitation "having an activity to bind to a human integrin selected from the group consisting of αvβ3, αvβ 5 and α9β1, which integrin is capable of binding to a full length human DANCE polypeptide", it is noted the support for such phrase can be found on page 63, line 20 to page 64, line 1 of the specification and Nakamura 2002 which is incorporated into the specification by reference.

Thus, for the above noted reasons, this rejection is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

Tomoyuki NAKAMURA et al.

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